inconsistency and thank the Examiner for bringing it to the Applicants attention. As stated on page 21 of the specification, the OX-43 antigen is know in the art as a marker for endothelial cells. (Appendix D) The data shown in Table 1 is contemporaneous data produced in the laboratory of the Applicants in which aortic endothelial cells were assessed for various cell surface markers. Notwithstanding the fact that is would be expected by one skilled in the art that aortic endothelial cells would be positive for the OX-43 antigen, Applicants recorded data to the contrary.

The Examiner has further objected to the specification contending that the reference on page 21, line 17 should be to Table 1 instead of Table 2 because "Table 2 does not recite any of the markers preceding the reference". Applicants have obviated this objection by amending the specification accordingly.

Objections to the Claims

The Examiner has identified various informalities in claims 1, 24 and 37. These claims have been amended as suggested by the Examiner, thereby obviating these objections.

Rejections Under 35 U.S.C. § 112, first paragraph

The Examiner has maintained his rejection based upon the contended lack of deposit of the recited cell lines. Upon indication of allowable subject matter herein, applicants will make any required deposits.

The Examiner has maintained his rejection of claim 24, contending that the claim reads gene therapy applications. The Examiner did state that this rejection would be overcome if the claim was amended to recite 'a method of producing a therapeutic polypeptide *in vitro*". (Office Action, page 5, first full paragraph) The Applicants thank the Examiner for his suggestion and have amended the claim accordingly. Applicants request that the rejection be withdrawn.

Rejections Under 35 U.S.C. § 112, second paragraph

The Examiner has rejected claims 1, 10 and 24 contending that the claims are indefinite. Specifically, claim 1 stands rejected because the Examiner contends it recites "improper Markush

language". Applicants have obviated the rejection by amending claim 1 to recite "consisting of" rather than "comprising" language.

Claim 10 also stands rejected. Applicants have obviated this rejection by amending claim 10 to correctly depend from claim 1 and to recite as the Examiner suggests "or" rather than "and" between the two cell lines.

Claim 24 stands rejected because the Examiner contends it recites "improper Markush language". Further, the Examiner has asked for clarification regarding the recited polypeptide and has suggested a clarifying amendment with respect to the order in which the claim is recited. Applicants have obviated the rejection by amending claim 24 to recite "consisting of" rather than "comprising" language and by amending the claim to make it clear which polypeptide is being described. Further, applicants have rearranged the claims language as suggested by the Examiner.

Rejections Under 35 U.S.C. § 103

Applicants acknowledge the obligation under 37 C.F.R. § 1.56 to "point out the inventor and the invention dates of each claim that was not commonly owned a the time a later invention was made".

Claims 1 and 24 stand "rejected under 35 U.S.C. § 103(a) as being unpatentable over Dunn et al (Invest Opthalmol Vis Sci (1998) 39:2744-2749)" ("Dunn"). Specifically, the Examiner contends that Dunn "teaches ARPE-19 comprising an expression vector encoding FGF5" and that, based on this supposed teaching, "it would have been obvious to express FGF2, rather than FGF5, using ARPE-19 cells". Solely in the efforts to facilitate prosecution Applicants have amended claims 1 and 24 to delete FGF2 from the Markush group. Applicants request that this rejection be withdrawn.

CONCLUSION

Applicants believe that the claims, as amended are in condition for allowance. If the Examiner has any questions, the Examiner is invites to contact the undersigned by telephone.

Respectfully submitted,

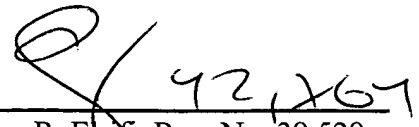

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TABLE 1 shows that the IO/JG2/1 clone expressed Von Willebrand's factor, the REC-1 antigen, the ICAM-1 antigen (the expression of which can also be induced by treatment with 100 U/ml of IFNγ or TNFα for 24 hr (TABLE 1; FIG. 4; and FIG. 6)), and the VCAM-1 antigen, after induction by the above-mentioned cytokines (200 U/ml of IFN γ or TNFα for 24 hr or 48 hr) (*cf.* TABLE 1).

(5) *Expression of endothelial markers specific for the CNS.* TABLE 1 also shows that the IO/JG2/1 clone constitutively expressed a number of markers specific for the endothelial cells of the CNS, especially P-glycoprotein, GLUT-1 and the transferrin receptor (*cf.* TABLE 1). However, the IO/JG2/1 clone did not express some of the antigens specific for the cerebral endothelial cells, especially the 1A8B and 2A4 antigens. This characteristic makes it possible to differentiate the IO/JG2/1 clone from the cerebral endothelium (TABLE 2 below).

(6) *Comparison of the expression of the endothelial antigens in the primary cultures and the lines with the peripheral endothelial cells.* As described above, the primary cultures of retinal endothelium and the derived clones expressing the T-antigen showed a constitutive expression of the markers specific for the endothelial cells of the CNS, namely P-glycoprotein, GLUT-1 and the transferrin receptor (TABLE 2), whereas the aortic endothelium does not express these antigens but does express the OX-43 antigen, which is considered to be specific for the peripheral endothelial cells. The OX-43 antigen was effectively not expressed either by the primary cultures or by the cultures of cerebral cells with extended life-span and the cultures of retinal endothelial cells with extended life-span (TABLE 1).

APPENDIX C

Claim Amendments in Bracket and Underline Form

1. (Twice amended) An injectable, non-tumorigenic, human retinal pigment epithelial cell line, wherein the cell line is selected from the group [comprising] consisting of hRPE-7, hRPE-116 and ARPE-19 and wherein the cells of the cell line:

(a) comprise an expression vector comprising a polynucleotide coding for a polypepeptide selected from the group [comprising] consisting of BDNF, NT-4, CNTF, Axokine, [FGF-2 (bFGF)], IGF I, IGF II, TGFβ-II, Midkine, IL-1β, TNF, NGF, IL-2/3, ILF, IL-6, NTN, Neublastin, VEGF, GDNF, PDGF, LEDGF and PEDF[.]; and

(b) can non-tumorigenically interact with retinal cells of a mammalian host.

10. (Twice amended) The cell line according to claim 1, wherein the cell line human retinal pigment epithelial-7 (hRPE-7) [and] or human retinal pigment epithelial-116 (hRPE-116).

24. (Twice amended) A method of producing a therapeutic polypeptide *in vitro* [to treat primary or secondary ophthalmologic or neurological disorders], comprising incubating cells of a mammalian retinal pigment epithelial cell line in a biologically compatible medium such that the cell line produces the polypeptide, wherein the cells of the cell line is selected from the group [comprising] consisting of hRPE-7, hRPE-116 and ARPE-19 [in a biological compatible medium such that the cell line produces the polypeptide] and wherein the cells of the cell line comprise an expression vector comprising a polynucleotide coding for [a] the polypeptide selected from the group [comprising] consisting of BDNF, NT-4, CNTF, Axokine, [FGF-2 (bFGF)], IGF I, IGF II, TGFβ-II, Midkine, IL-1β, TNF, NGF, IL-2/3, ILF, IL-6, NTN, Neublastin, VEGF, GDNF, PDGF, LEDGF and PEDF.

37. (Twice amended) The cell line IO/JG2/1, deposited under I-1695 on April 18, 1996 in the Collection Nationale de Cultures de Micro-organismes held by the Insitut[e] Pasteur, Paris France.

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☐ 1: Immunology 1986 Feb;57(2):231-7

MRC OX-43: a monoclonal antibody which reacts with all vascular endothelium in the rat except that of brain capillaries.

Robinson AP, White TM, Mason DW.

A mouse monoclonal antibody, MRC OX-43, has been shown to label vascular endothelium in all tissues of the rat except that of brain capillaries. Using immunoperoxidase staining, the antigen was shown to be expressed on the luminal surface of blood vessels. In addition, this antibody recognized a surface antigen on circulating erythrocytes and some macrophage populations, namely all those in the peritoneal cavity and a subset of alveolar macrophages. The antigen recognized by this antibody was identified on macrophages by metabolic and cell surface labelling followed by immunoprecipitation and sodium dodecyl sulphate polyacrylamide gel electrophoresis (SDS-PAGE) and found to be a surface protein of 90,000 MW.

PMID: 2936678 [PubMed - indexed for MEDLINE]